**DETAILED ACTION**

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 8/10/09 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/9/09 has been entered.

Claims 17 and 22 have been amended.

Claims 17-27 are pending.

Claims 20-22 and 25 stand withdrawn from further consideration pursuant to 37 CFR 1.14209 as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 17-19, 23-24, and 26-27 are under examination.

2. Upon reconsideration and in view of Applicant's remarks, the rejection of claim 26 under 35 U.S.C. 112 first paragraph for new matter is withdrawn.

3. The rejection of the claims under 35 U.S.C. 112 first paragraph for lack of enablement is withdrawn in view of Applicant's amendment to the claims.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17, 19, 23-24, and 26-27 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is

insufficient written description to demonstrate that applicant was in possession of the claimed genus of glutamate "analogs".

As set forth previously, The instant claims are drawn to a method employing a glutamate "analog" that stimulates glutamate receptor activation, as measured by upregulation of T-cell cytokine secretion, adhesion, or chemotactic migration. Glutamate receptor exists as a myriad of different subtypes (for example there are three types of ionotropic receptors, and at least 8 different metabotropic glutamate receptors). Furthermore, it is noted that a "substantial" identity is completely relative, and the specification does not provide any guidance as to what structural features are required (for example, the specification does not disclose a required core chemical structure or examples of functional groups that might be altered). Therefore, the specification does not provide a correlation between the structure of the glutamate "analogs" and the function of stimulating any glutamate receptor. The specification on page 33 discloses 5 glutamate analogs. The 5 compounds are not representative of the broad range of analogs encompassed by the claims, which act as agonists for any glutamate receptor, including the 8 metabotropic receptors as well as the numerous ionotropic types of receptors. Additionally, even when the claims are limited to analogs that stimulate the GluR3 receptor, the specification only discloses a single species of said analog, AMPA. A single species is not sufficiently representative of the broad genus of GluR3 analogs encompassed by the claims. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

Applicant's arguments filed 3/9/09 have been fully considered, but they are not persuasive.

Applicant argues that the 5 species of analog disclosed by the specification are sufficient to demonstrate that applicant was in possession of the entire genus.

The 5 compounds disclosed by the specification are not sufficiently representative of the broad range of analogs encompassed by the claims, which include those that act as agonists for up to any of the 11 known glutamate receptors. Additionally, the specification does not provide any guidance as to what structural features of the claimed analogs correlate with the function of upregulating the claimed T cell activities. In fact, the specification does not even disclose which glutamate receptors correlate with the function of stimulating T cell activity (i.e. there is no correlation between the structure of the glutamate receptors or analogs and the function of stimulating T cell activity).

Applicant further argues that any given analog could be readily tested to determine whether or not it has the properties required.

However, the disclosure of a method to identify the analogs of the claims does not provide any information regarding what structural features would be associated with the ability to upregulate T cell activity.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-18, 23-24, and 26-27 stand rejected under 35 U.S.C. 102(b) as being anticipated by Winter et al., 1999, as evidenced by Droge et al. 1988 (of record).

As set forth previously, Winter et al. teach a method of enhancing the anti-tumor T cell response (i.e. a method of upregulating a "T cell activity") comprising administering T cells to a subject with a tumor (see page 4465 in particular). Winter et al. further teach that the T cells are cultured ex-vivo in RPMI medium before administration (see page 4463 in particular). As evidenced by Droge et al., RPMI medium contains glutamate (see pages 126-127). Thus, Winter et al. have inherently treated the T cells ex-vivo with glutamate, as recited in the instant claims. Said glutamate treatment would inherently stimulate the glutamate receptor, including the GluR3 receptor.

Applicant's arguments filed 3/9/09 have been fully considered, but they are not persuasive.

Applicant argues that as evidenced by Ganor et al., activation of T cells is only obtained with glutamate in the 10 nM range and not at higher concentrations like those that are present in RPMI (as used by Winter et al.). Thus, Applicant concludes that Winter et al. do not teach stimulation with a molecule "in an amount sufficient to stimulate glutamate receptor activation".

In the secondary evidentiary reference provided by Applicant (Poulopoulou and Levite), it is noted that the experiments of Ganor et al. were performed using RPMI which contains glutamate. The reference postulates that since the RPMI used in the experiments was stored for prolonged periods, the glutamate concentration might have disappeared due to the instability of glutamate in solution. The reference does not provide any information as to the actual glutamate concentration of the RPMI used in the experiments. Thus, it appears that no conclusions can be drawn as to which

concentrations of glutamate are sufficient to stimulate glutamate receptor activation based on Ganor et al., since the actual glutamate concentrations in the experiments of Ganor et al. are not known. Additionally, the cited references only study the effect of glutamate concentration of the ability of T cells to adhere to fibronectin, while the instant claims encompass a range of other T cell activities. Thus, Applicant has not provided sufficient evidence to demonstrate that the concentration of glutamate present in RPMI (as used by Winter et al.) would be too high to result in upregulation of T cell cytokine secretion, T cell adhesion, or T cell chemotactic migration. In fact, Winter et al. teach that the cultured T cells upregulate the production of IFN-gamma (i.e. upregulate cytokine secretion, see Fig. 6). Furthermore, as evidenced by Droge et al., higher concentrations of glutamate (up to 500 uM) can effect lymphocyte function, which indicates that even high concentrations of glutamate can stimulate glutamate receptor activation, as recited in the instant claims. Additionally, it is noted that the instant claims are not limited to a particular glutamate concentration. Thus, the method of Winter et al. meets all the limitations of the instant claims, including treating T cells with an amount of glutamate sufficient to stimulate glutamate receptor activation, as recited in the instant claims.

6. No claim is allowed.

1. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, whose telephone number is 571-272-4471. The examiner can normally be reached on 7am to 3:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Amy E. Juedes
Patent Examiner
Technology Center 1600
/Amy E. Juedes/
Patent Examiner, Art Unit 1644